## REMARKS/ARGUMENTS

With this amendment, claims 43 and 46 are pending. Claims 1-42, 44-45, and 47-51 are cancelled without prejudice. For convenience, the Examiner's rejections are addressed in the order presented in an October 18, 2007, Office Action.

Applicants thank Examiner Swope for her time and assistance in participating in a telephonic interviews with Applicants' representative Beth Kelly on October 11 and 12, 2007. The previously filed response was deemed non-responsive and agreement for proceeding with prosecution was reached and is reflected in this response and a previously filed supplementary response.

### I. Status of the claims

Claims 43 and 46 are amended to recite a β1,4-N-acetylgalactosaminyl (GalNAc) transferase polypeptide encoded by a nucleic acid that can be amplified by primers that bind to the 3' and 5' end of the *C. jejuni* LOS locus. Support for β1,4-GalNAc transferase proteins encoded by the *C. jejuni* LOS locus is found throughout the specification, for example, at page 53, line 14 through page 56, line 4. Claim 43 also recites that the β1,4-GalNAc transferase transfers a GalNAc residue from a donor substrate to an acceptor substrate. Support for β1,4-GalNAc transferase activity is found throughout the specification, for example, at page 20, lines 16-18; page 23, line 12 through page 24, line 16; and page 50, lines 2-14.

### II. Rejections under 35 U.S.C. §101

Claims 43 is rejected for alleged lack of utility because they recite β1,4-N-acetylglucosaminyl (GalNAc) transferase activity. Applicants have amended claim 43 to correct a typographical error and, to the extent the rejection applies to the amended claims, Applicants respectfully traverse. Claim 43 is amended to recite a β1,4-N-acetylgalactosaminyl (GalNAc) transferase polypeptide, as is its dependent claim 46. Support for β1,4-N-acetylgalactosaminyl transferase activity is found in the specification at page 20, lines 16-18; page 23, line 12 through page 24, line 16; and page 50, lines 2-14. Experimental evidence of β1,4-N-

acetylgalactosaminyl transferase activity is found, *e.g.*, at page 67, line 8 through page 68, line 2 and at Figure 4. In view of the amendment and remarks, withdrawal of the rejection for alleged lack of utility is respectfully requested. Applicants believe the amendment and remarks are also sufficient to address a related rejection for alleged lack of enablement.

**III. Rejections under 35 U.S.C. §112, second paragraph**

Claim 46 is rejected for alleged indefiniteness. Claim 46 is now amended to depend from claim 43. In view of this amendment, withdrawal of the rejection for indefiniteness is respectfully requested.

**IV. Rejections under 35 U.S.C. §112, first paragraph, enablement**

Claims 43 is rejected under 35 U.S.C. §112, for allegedly failing to provide enablement for any protein with glycosyltransferase activity or β1,4-N-acetylglucosaminyl (GalNAc) transferase activity encoded by a nucleic acid that can be generated by PCR using primers of SEQ ID NO:40 and 41 using *Campylobacter* genomic DNA as a template. In order to expedite prosecution, claim 43 is amended to recite a polynucleotide sequence that encodes a β1,4-N-acetylgalactosaminyl (GalNAc) transferase polypeptide. The Office Action also alleges that undue experimentation is required to practice the claimed invention. To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection.

Factors such as the amount of guidance presented in the specification and the presence of working examples must be considered to determine whether undue experimentation is required to practice the claimed invention. *See, e.g.*, *Ex Parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). As described in *Wands*, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Wands*, USPQ2d at 1404, quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982). Moreover, "[a] patent need not teach, and preferably omits, what is well known in the art." MPEP 2164.01 *citing In re Buchner*, 18

USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 221 USPQ 481, 489 (Fed. Cir. 1984).

As set forth in the Manual of Patent Examining Procedure (MPEP) § 2164.01, "the test of enablement is not whether any experimentation is necessary, but whether… it is undue." Further, the "fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation" (citations omitted). Finally, claims reading on inoperative embodiments are enabled if the skilled artisan understands how to avoid inoperative embodiments. *See, e.g., In re Cook and Merigold*, 169 USPQ 299, 301 (C.C.P.A. 1971).

Arguments in the previously filed response were not deemed persuasive, first because the specification allegedly does not provide evidence of the structure of a β1,4-N-GalNAc transferase, does not provide evidence that an exemplified β1,4-N-GalNAc transferase protein has the recited activity, and does not disclose a β1,4-N-GalNAc transferase protein encoded by a polynucleotide that can be amplified by PCR using primers of SEQ ID NO: 40 and 41.

Applicants respectfully request the Examiner to consider the following evidence from the specification. First, the specification at page 23, line 12 through page 24, line 9 discloses that SEQ ID NO:17 is a β1,4-N-GalNAc transferase protein. The sequence listing provides additional β1,4-N-GalNAc transferase amino acid sequences and encoding nucleic acid sequences at SEQ ID NOs:18-25. Thus, the specification does disclose the structure of multiple β1,4-N-GalNAc transferase proteins. β1,4-N-GalNAc transferase activity is asserted at, *e.g.*, page 23, lines 13-16.

β1,4-N-GalNAc transferase activity is asserted at, *e.g.*, page 23, lines 13-16 and the specification also provides experimental evidence that the β1,4-N-GalNAc transferase protein of *C. jejuni* strain OH4384 does indeed have β1,4-N-GalNAc transferase activity. *See, e.g.*, specification at page 50, lines 2-4 and page 56, lines 8-14. The β1,4-N-GalNAc transferase substrate is a fluorescent molecule called GM3-FCHASE and the product is called GM2-

FCHASE. Figure 4 shows the reaction pathway, including formulas of the acceptor substrates and product, *i.e.*, GM3 and GM2. The β1,4-N-GalNAc transferase protein I figure 4 is referred to as CgtA. The inventors performed through and detailed analysis of the β1,4-N-GalNAc transferase reaction products, *i.e.*, fluorescently labeled FCHASE molecules, to confirm that the recited activity is correct. NMR analysis of the product is disclosed at page 57, lines 1-4 and table 4. Additional mass determination of the product is disclosed at page 67, line 8 through page 69, line 2. Thus, the specification provides disclosure of the reaction conditions to assay β1,4-N-GalNAc transferase activity and verification that transfer of GalNAc from a donor substrate to an acceptor substrate does occur.

The Office Action also alleges that the specification does not disclose a β1,4-N-GalNAc transferase protein encoded by a polynucleotide that can be amplified with primers of SEQ ID NO:40 and 41. Applicants respectfully disagree and assert that the specification does disclose β1,4-N-GalNAc transferase proteins encoded by nucleic acids that can be amplified from a *C. jejuni* genome using primers SEQ ID NO:40 and 41. The application is based on the inventors' recognition that a particular region of the *C. jejuni* genome, the LOS locus, encodes glycosyltransferases that produce the oligosaccharide structures found on the outer surface of the bacterium. The inventors produced primers that hybridize to conserved sequences at the 5' and 3' ends of the LOS locus, *i.e.*, SEQ ID NO:40 and 41. The primers were used to amplify the entire LOS region of a *C. jejuni* genome from strain OH4384. *See, e.g.*, specification at page 45, lines 22-26. PCR conditions are described at page 46, line 26 through page 47, line 6 and page 48, lines 1-9. The organization of genes from the LOS locus of two strains is depicted in Figure 2B. The nucleic acid referred to as ORF 5a encodes a β1,4-N-GalNAc transferase, as indicated by Table 3. Thus, primers of SEQ ID NO:40 and 41 can be used to PCR amplify a nucleic acid that encodes a β1,4-N-GalNAc transferase protein from a *C. jejuni* genome.

The Office Action secondly deems previously presented arguments unpersuasive because the specification allegedly fails to establish certain characteristics of the claimed β1,4-N-GalNAc transferase proteins. Part of the Office Action's arguments are based on a typographical error: use of β1,4-N-acetylglucosaminyl (GalNAc) transferase, rather than β1,4-N-

acetylgalactosaminyl (GalNAc) transferase. Use of the term GalNAc as an abbreviation of N-acetylgalactosaminyl is found in the specification at page 10, line 25. Applicants have corrected the claims to recite β1,4-N-acetylgalactosaminyl (GalNAc) transferase and arguments are based on this correction.

According to the Office Action the specification does not provide the structure of a protein that has β1,4-N-acetylglucosaminyl (GalNAc) transferase. As indicated above, Applicants have corrected the claims to recite β1,4-N-acetylgalactosaminyl (GalNAc) transferase and the sequence of multiple β1,4-N-GalNAc transferase proteins and their encoding nucleic acids are found in the application, for example, at SEQ ID NOs:16-25. The disclosed β1,4-N-GalNAc transferase nucleic acids originated from the LOS locus of *C. jejuni* genomes. As indicated above, the specification teaches that LOS loci can be amplified using primers of SEQ ID NO:40 and 41. Thus, the specification does disclose β1,4-N-GalNAc transferase nucleic acids that can be amplified from a *C. jejuni* genome and the proteins encoded those nucleic acids.

According to the Office Action, the specification does not disclose the specific type of glycosyltransferase activity of all proteins that are encoded by any polynucleotide that can be generated from any Campylobacter cell using primers of SEQ ID NO:40 and 41 and does not disclose which Campylobacter cells can be used with the primers. Applicants respectfully disagree. First, the claims are directed to proteins that have β1,4-N-GalNAc transferase activity, *i.e.*, proteins that transfer a GalNAc residue from a donor substrate to an acceptor substrate. The activity of other proteins encoded by nucleic acids from the LOS locus is not relevant to the pending claims. Nevertheless, Applicants respectfully direct the Examiner's attention to Figure 2B and Table 3, which provide the organization of representative LOS loci and functional information on gene products for the LOS locus from *C. jejuni* strain OH4384. Exemplary *C. jejuni strains*, such as O:19, including OH4384 and OH4382; O:10, O:41, and O:2; are disclosed throughout the specification, for example, at page 22, lines 14-18; page 46, lines 20-24; and in the sequence listing.

According to the Office Action the specification fails to provide a rational and predictable scheme for isolating protein with the desired activity. Applicants respectfully

disagree. The specification does provide guidelines for those of skill to isolate a protein with the claimed activity. First, the specification discloses the LOS core oligosaccharide structures of a number of *C. jejuni* strains at Figure 1. The specification provides assays for the activity of the claimed β1,4-N-GalNAc transferase proteins. The donor saccharides, acceptor saccharides, and oligosaccharide products are disclosed at, *e.g.*, page 23, lines 13-19. Assay conditions are disclosed at, *e.g.*, page 50, lines 2-4. The assays were performed using synthetic fluorescent oligosaccharides as acceptors and are sensitive enough to assay crude fractions from *C. jejuni* cells for β1,4-N-GalNAc transferase activity. *See, e.g.*, specification at page 52, lines 1-12. If β1,4-N-GalNAc transferase activity was present in a crude fraction, the *C. jejuni* LOS loci were sequenced with the expectation of finding a β1,4-N-GalNAc transferase encoding nucleic acid at the LOS locus. Primers of SEQ ID NO:40 and 41 are disclosed and are used to sequence an LOS locus. *See, e.g.*, specification at page 48, lines 1-12 and Table 2. Reference β1,4-N-GalNAc transferase amino acid and nucleic acid sequences are provided at SEQ ID NO:16-25. These sequences can be used by those of skill to further identify β1,4-N-GalNAc transferase nucleic acid and amino acid sequences. As an example, the *C. jejuni* strain OH4384 has an active β1,4-N-GalNAc transferase (SEQ ID NO:17) encoded by the LOS locus. The inventors also sequenced closely related amino acid sequence in the *C. jejuni* strain OH4392 and found that it had a frame-shift mutation, resulting in a 27 amino acid protein, rather than the 347 amino acid protein of the OH4384 strain. The inventors recognized that the 27 amino acid protein would not be functional. *See, e.g.*, specification at page 57, lines 1-11. Those of skill would reach the same conclusion. Thus, using the assays and sequence information provided in the specification, those of skill can identify, make, and use the claimed β1,4-N-GalNAc transferase proteins.

The Office Action alleges that the specification fails to provides sufficient guidance to find successful candidates out of allegedly "essentially infinite possible choices." Office Action at page 5. Applicants respectfully disagree. The choices for those of skill are not infinite. The specification, as discussed above, provides sensitive β1,4-N-GalNAc transferase assays that can be used to preliminarily identify *C. jejuni* strains that have a β1,4-N-GalNAc transferase protein encoded by a nucleic acids that can be amplified from the LOS locus of the

genome. As discussed in the previous response, the specification demonstrates that large scale screens for a glycosyltransferase activity are routinely done by those of skill. This techniques can be used, to screen large numbers of *C. jejuni* strains for activity, or once an appropriate *C. jejuni* strain is identified, can be used during cloning in, *e.g.*, an *E. coli* bacterium to screen large numbers of candidates for a nucleic acid that encodes a β1,4-N-GalNAc transferase protein. The specification provides primers 40 and 41. Productive amplification using those primers will occur only from the genome of *C. jejuni* strains that have an LOS locus with sequences complementary to the primers. β1,4-N-GalNAc transferase reference nucleic acid and amino acid sequences are also disclosed at SEQ ID NOs:16-25. Computer programs are available to identify related sequences. Again, those of skill can use the β1,4-N-GalNAc transferase assays in the specification to identify proteins with the recited activity. Therefore, the possibilities are not infinite and those of skill can identify the claimed proteins, using at most, routine experimentation.

In view of the above amendments and arguments, withdrawal of the rejection for alleged lack of enablement is respectfully requested.

## V. Rejections under 35 U.S.C. §112, first paragraph, written description

Claims 43 is rejected under 35 U.S.C. §112, for allegedly containing subject matter that was not described in the specification as filed. The Office Action alleges that those of skill would not recognize that the inventors had possession of the claimed genus at the time of filing. The claims are now amended to recite β1,4-N-acetylgalactosaminyl (GalNAc) transferase, rather than β1,4-N-acetylglucosaminyl (GalNAc) transferase. To the extent the rejection applies to the amended claims, Applicants respectfully traverse.

As currently applied, the specification does comply with US patent law for description of a nucleic acid or amino acid sequence. The Federal Circuit court of Appeals addressed the description adequate to show one of skill that the inventors were in possession of a claimed genus at the time of filing. *See, e.g., Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 63 USPQ2d 1609 (Fed. Cir. 2002). An applicant may also show that an invention is complete by

> . . . disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention . . . *i.e.*, complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *Id.* at 1613.

Furthermore, "description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces." *See, e.g.*, 66 Fed. Reg. 1099, 1106 (2001).

The specification does provide descriptive support for the full scope of the claimed genus by providing a representative number of species of β1,4-GalNAc transferase amino acid sequences and encoding nucleic acid sequences, *e.g.*, SEQ ID NOs:16-25, and a β1,4-GalNAc transferase assay used to determine whether polypeptides have the enzymatic activity required by the claims. The assay is described at page 20, lines 16-18; page 23, line 12 through page 24, line 16; and page 50, lines 2-14. This information is more than adequate to meet the written description requirement, particularly in view of *Enzo*, cited above, recent Board decisions, and the interpretation of the Written Description Guidelines evidenced by the USPTO's own Synopsis of Application of Written Description Guidelines.

In view of the above arguments and amendments, withdrawal of the rejection for alleged lack of written description is respectfully requested.

## CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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